

WHAT IS CLAIMED IS:

1. A Nogo protein that is free of all central nervous system myelin material
5 with which it is natively associated.

2. The protein of claim 1 which is selected from the group consisting of
Nogo A and Nogo B.

10 3. The protein of claim 2 which comprises the amino acid sequence of
Figure 2a (SEQ ID NO: 2).

4. The protein of claim 2, the amino acid sequence of which consists of an
amino acid sequence selected from the group consisting of residues 1-1163 depicted in
15 Figure 2a (SEQ ID NO: 2), and residues 1-172 fused to 975-1163 depicted in Figure 2
(SEQ ID NO: 2).

5. A purified Nogo C protein.

20 6. The protein of claim 5, which comprises the amino acid sequence of
SEQ ID NO: 32 depicted in Figure 14.

7. The protein of claim 5, the amino acid sequence of which consists of
SEQ ID NO: 32 depicted in Figure 14.

25

8. The protein of claim 2 or 5 which is recombinantly produced.

9. The protein of claim 2 or 5 which has the sequence of a mammalian
protein.

30

10. The protein of claim 1, 2 or 5 which has the sequence of a human
protein.

11. A protein comprising an amino acid sequence that has at least one
35 conservative amino acid substitution in the amino acid sequence depicted in Figure 2a (SEQ
ID NO:2), the amino acid sequence depicted in Figure 13 (SEQ ID NO:30) or the amino

acid sequence depicted in Figure 14 (SEQ ID NO:32), and which is able to be bound by an antibody directed against a Nogo protein having an amino acid sequence selected from the group consisting of residues 1-1163 of SEQ ID NO: 2, residues 1-172 fused to 975-1163 of SEQ ID NO: 2, and residues 1-199 of SEQ ID NO: 32.

12. The protein of claim 1 which comprises an amino acid sequence that is displaying a greater than 50% homology to the amino acid sequence of SEQ ID NO:2, as determined by a BLAST computer algorithm.

13. The protein of claim 1 which is encoded by a first nucleic acid that is hybridizable to a second nucleic acid having the nucleotide sequence depicted in Figure 2a (SEQ ID NO:1) or the nucleotide sequence depicted in Figure 12 (SEQ ID NO:28).

14. A purified fragment of the protein of claim 1 which is able to be bound by an antibody directed against a Nogo protein, and wherein said purified fragment is free of all central nervous system myelin material.

15. A purified fragment of the protein of claim 5 or 11 which is able to be bound by an antibody directed against a Nogo protein.

16. A purified protein comprising a fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of residues 31-57 depicted in Figure 2a (SEQ ID NO:2), the residues 11-191 depicted in Figure 14 (SEQ ID NO:32), the residues 988-1023 depicted in Figure 2a (SEQ ID NO:2), and residues 1090-1125 depicted in Figure 2a (SEQ ID NO:2), residues 994-1174 depicted in Figure 13 (SEQ ID NO:30), residues 977-1012 depicted in Figure 13 (SEQ ID NO:30), and residues 1079-1114 depicted in Figure 13 (SEQ ID NO:30).

17. A purified unglycosylated protein which is selected from the group consisting of Nogo A, Nogo B and Nogo C.

18. A purified protein that is free of all central nervous system myelin material and that is encoded by a first nucleotide sequence that is hybridizable to a second nucleic acid, said second nucleic acid having a nucleotide sequence depicted in Figure 2a (SEQ ID NO:1) or a nucleotide sequence depicted in Figure 12 (SEQ ID NO:28), which

protein is able to be bound by an antibody directed against a second protein having an amino acid sequence depicted in Figure 2a (SEQ ID NO:2).

19. A chimeric protein comprising a fragment of the protein of claim 2, 5, or 11 which is able to be bound by an antibody directed against a Nogo protein, fused by a covalent bond to at least a portion of a second protein, which said second protein is different from said fragment of protein of claim 2, 5, or 11.

20. A purified molecule comprising a fragment of the protein of claim 1 which is able to be bound by an antibody directed against a Nogo protein, and wherein said purified molecule is free of all central nervous system myelin material.

21. A purified molecule comprising a fragment of the protein of claim 5, or 11 which is able to be bound by an antibody directed against a Nogo protein.

22. An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:33.

23. An isolated nucleic acid comprising:

(a) a nucleotide sequence that encodes a polypeptide having an amino acid sequence selected the group consisting of residues 1-1163 depicted in Figure 2a (SEQ ID NO:2), residues 1-172 fused to 975-1163 depicted in Figure 2a (SEQ ID NO:2), and residues 1-199 depicted in Figure 14 (SEQ ID NO:32); or

(b) the complement of the nucleotide sequence of (a).

24. An isolated first nucleic acid capable of hybridizing to a second nucleic acid, said second nucleic acid having a nucleotide sequence complementary to a nucleotide sequence that encodes a polypeptide having an amino acid sequence selected from the group consisting of residues 1-1163 depicted in Figure 2a (SEQ ID NO:2), residues 1-172 fused to 975-1163 depicted in Figure 2a (SEQ ID NO:2), and residues 1-199 depicted in Figure 14 (SEQ ID NO:32); and encodes a naturally occurring protein that is able to be bound by an antibody to a protein having an amino acid sequence of SEQ ID NO: 2.

25. The isolated nucleic acid of claim 24 which encodes a naturally occurring human Nogo protein.

26. An isolated first nucleic acid that is hybridizable to a second nucleic acid, said second nucleic acid having a nucleotide sequence depicted in Figure 2a (SEQ ID NO:1) or a nucleotide sequence depicted in Figure 12 (SEQ ID NO:28), and wherein said first nucleic acid encodes a first protein that is able to be bound by an antibody directed against a second protein having an amino acid sequence depicted in Figure 2a (SEQ ID NO:2).

27. An isolated nucleic acid that encodes a naturally occurring protein that is able to be bound by an antibody to a protein having an amino acid sequence of SEQ ID NO: 2, and that has a greater than 70% nucleotide sequence homology to a nucleotide sequence that encodes a polypeptide having an amino acid sequence selected from the group consisting of residues 1-1163 of SEQ ID NO:2, residues 1-172 fused to 975-1163 of SEQ ID NO:2, and residues 1-199 of SEQ ID NO:32, as determined by a BLAST computer algorithm.

28. The nucleic acid of claim 27 in which the naturally occurring protein is a human protein.

29. An isolated nucleic acid comprising a nucleotide sequence encoding a fragment of a Nogo protein that displays one or more functional activities of the Nogo protein, wherein said Nogo protein is not a human Nogo protein, a Drosophila Nogo protein or a Nogo protein of Caenorhabditis elegans.

30. An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising an amino acid sequence that has a greater than 50% homology to the amino acid sequence of SEQ ID NO:30, as determined by a BLAST computer algorithm.

31. An isolated nucleic acid that encodes at least 220 continuous amino acid residues of the amino acid sequence of SEQ ID NO:2.

32. An isolated nucleic acid that comprises the nucleotide sequences of at least two non-overlapping human expressed sequence tags selected from the group consisting of: AA158636 (SEQ ID NO:35), AA333267 (SEQ ID NO:36), AA081783 (SEQ ID NO:37), AA167765 (SEQ ID NO:38), AA322918 (SEQ ID NO:39), AA092565 (SEQ ID NO:40), AA081525 (SEQ ID NO:41), and AA081840 (SEQ ID NO:42).

33. A vector comprising the nucleic acid of any one of claims 22, 23, 24, and 25 operably linked to a non-native promoter.

34. An expression vector comprising the nucleic acid of any one of claims 22, 23, 24, and 25.

35. A recombinant cell transformed with the nucleic acid of any one of claims 22, 23, 24, and 25.

36. The recombinant cell of claim 35 which is a prokaryotic recombinant cell.

37. The recombinant cell of claim 35 which is a eukaryotic recombinant cell.

38. A method of producing a recombinant protein comprising culturing a recombinant cell transformed with the nucleic acid of claim 22, 23, 24, or 25 such that a protein encoded by the nucleic acid is expressed by the cell, and recovering the expressed protein.

39. The method of claim 38 wherein the recombinant cell is a prokaryotic recombinant cell.

40. The method of claim 38 wherein the recombinant cell is an eukaryotic recombinant cell.

41. A method of treating a subject with a neoplastic disease of the central nervous system comprising administering to the subject a therapeutically effective amount of a Nogo protein or a fragment thereof, that is free of all central nervous system myelin material with which the Nogo protein is natively associated, said fragment being active in inhibiting cell proliferation.

42. The method of claim 42 in which the neoplastic disease is glioma, glioblastoma, medulloblastoma, craniopharyngioma, ependyoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, or retinoblastoma.

102
126-

43. The method of claim 42 in which the subject is a human.

44. A method of treating a subject with damage to the central nervous system comprising administering to the subject a therapeutically effective amount of a
5 ribozyme or an antisense Nogo nucleic acid that inhibits the production of Nogo in the subject.

45. A method of inducing regeneration or sprouting of neurons in a subject comprising administering to the subject a therapeutically effective amount of a ribozyme or
10 an antisense Nogo nucleic acid that inhibits the production of Nogo in the subject.

46. A method of promoting structural plasticity of the central nervous system of a subject comprising administering to a subject in whom structural plasticity of the central nervous system is desired a therapeutically effective amount of a ribozyme or an
15 antisense Nogo nucleic acid that inhibits the production of Nogo in the subject.

47. A recombinant non-human animal that is the product of a process comprising introducing a nucleic acid encoding at least a domain of a Nogo protein into the genome of the animal, or a progeny of said animal.
20

48. A recombinant non-human animal in which a *Nogo* gene has been inactivated or deleted.

49. The animal of claim 48 in which the *Nogo* gene has been inactivated by
25 a method comprising introducing a nucleic acid into the animal or an ancestor thereof, which nucleic acid comprises a non-Nogo gene sequence flanked by Nogo gene sequences that promote homologous recombination.

50. A purified fragment of a Nogo protein comprising an amino acid
30 sequence selected from the group consisting of amino acid residues 1-171, 172-974, 259-542, 542-722, 172-259, 722-974, and 975-1162 of SEQ ID NO: 2, that is free of all central nervous system myelin material.

51. A purified fragment of a Nogo protein that lacks amino acid residues
35 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of

173

SEQ ID NO:2 but otherwise comprises the remainder of SEQ ID NO: 2, and that is free of all central nervous system myelin material.

52. A purified fragment of a Nogo protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO: 30, that is free of all central nervous system myelin material.

53. A purified fragment of a Nogo protein that lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:30 but otherwise comprises the remainder of SEQ ID NO: 30, and that is free of all central nervous system myelin material.

54. A purified protein comprising a fragment of a Nogo protein, which protein (a) lacks amino acid residues 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of SEQ ID NO:2; and (b) displays the neurite growth inhibitory activity of said Nogo protein, and is free of all central nervous system myelin material.

55. A purified protein comprising a fragment of a Nogo protein, which protein (a) lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:30; and (b) displays the neurite growth inhibitory activity of said Nogo protein, and is free of all central nervous system myelin material.

25

56. An isolated nucleic acid that encodes a protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-171, 172-974, 259-542, 542-722, 172-259, 722-974, and 975-1162 of SEQ ID NO: 2.

57. An isolated nucleic acid that encodes a protein that lacks amino acid residues 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of SEQ ID NO:2 but otherwise comprises the remainder of SEQ ID NO: 2.

58. An isolated nucleic acid that encodes a protein comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO: 30.

104
178

59. An isolated nucleic acid that encodes a protein that lacks amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:30 but otherwise comprises the remainder of SEQ ID NO: 30.

5

59.

60. A vector comprising the nucleic acid of any one of claims 56, 57, 58 and

61. A recombinant cell transformed with the nucleic acid of any one of claims 56, 57, 58 and 59.

10

62. A fusion protein comprising the fragment of claim 52, 53, or 55 fused to an amino acid sequence of a non-Nogo protein.

20

25

30

35

T04260" EX000000

175
59-